Data Evaluation Report on the Acute Oral Toxicity of DPX-MAT28 Technical (Aminocyclopyrachlor) to Northern Bobwhite Quail (*Colinus virginianus*)

PMRA Submission Number {.....} EPA MRID Number 47560118

Data Requirement:	PMRA Data Code	{.....}
	EPA DP Barcode	358148
	OECD Data Point	{.....}
	EPA MRID	47560118
	EPA Guideline	850.2100

Test material: DPX-MAT28 Technical **Purity:** 92.2%
Common name Aminocyclopyrachlor
Chemical name:
IUPAC: 6-amino-5-chloro-2-cyclopropylpyrimidine-4-carboxylic acid
CAS: 6-amino-5-chloro-2-cyclopropyl-4-pyrimidinecarboxylic acid
CAS No.: 858956-08-8
Synonyms: None reported

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Date: 07/06/09

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Date: 10/05/09

Reference/Submission No.: {.....}

Company Code	{.....}	[For PMRA]
Active Code	{.....}	[For PMRA]
Use Site Category	{.....}	[For PMRA]
EPA PC Code	None	

Date Evaluation Completed: 10/05/09

CITATION: Gallagher, S.P., and J.B. Beavers. 2007. DPX-MAT28 Technical: An Acute Oral Toxicity Study with the Northern Bobwhite. Unpublished study performed by Wildlife International Ltd., Easton, MD. Laboratory Project No. 112-599. Study sponsored by E.I. du Pont de Nemours and Company, Wilmington, DE. Study initiated March 23, 2007 and submitted August 22, 2007.

DISCLAIMER: This document provides guidance for EPA and PMRA reviewers on how to complete a data evaluation record after reviewing a scientific study concerning the acute oral toxicity of a pesticide to avian species. It is not intended to prescribe conditions to any external party for conducting this study nor to establish absolute criteria regarding the assessment of whether the study is scientifically sound and whether the study satisfies any applicable data requirements. Reviewers are expected to review and to determine for each study, on a case-by-case basis, whether it is scientifically sound and provides sufficient information to satisfy applicable data requirements. Studies that fail to meet any of the conditions may be accepted, if appropriate; similarly, studies that meet all of the conditions may be rejected, if appropriate. In sum, the reviewer is to take into account the totality of factors related to the test methodology and results in determining the acceptability of the study.

EXECUTIVE SUMMARY:

The acute oral toxicity of DPX-MAT28 Technical (aminocyclopyrachlor) to 20-week old Northern bobwhite quail (*Colinus virginianus*) was assessed over 14 days. DPX-MAT28 was administered to the birds by gavage at nominal levels of 0 (vehicle control), 269, 448, 747, 1245, and 2075 mg ai/kg bw (limit dose). No treatment-related mortality, clinical signs of toxicity, or effects on body weight or food consumption were indicated during the study. The 14-day acute oral LD_{50} was >2075 mg ai/kg bw and the 14-day NOAEL was 2075 mg ai/kg bw. DPX-MAT28 Technical (aminocyclopyrachlor) is classified as practically non-toxic to young adult Northern bobwhite quail (*Colinus virginianus*) on an acute oral basis, in accordance with the classification system of the U.S. EPA.

This toxicity study is scientifically sound and classified as acceptable and, thus, satisfies the guideline requirement for an acute oral toxicity study with Northern bobwhite quail.

Results Synopsis

Test Organism Size/Age (Mean Weight): 20-weeks old; 168 to 221 g (combined sexes)

LD_{50}: >2075 mg ai/kg bw	95% C.I.: N/A
Probit slope: N/A	95% C.I.: N/A
NOAEL: 2075 mg ai/kg bw	
Endpoint(s) Affected: none	

I. MATERIALS AND METHODS

GUIDELINE FOLLOWED: U.S. EPA Ecological OPPTS No. 850.2100 (1996)
U.S. EPA Pesticide Assessment Guidelines, §71-1 (1982)

Deviations from OPPTS 850.2100 included:

1. The pre-test health of the population (including mortality) was not reported.
2. Two males and two female birds did not meet the minimum weight requirement of 180 g at study initiation.

These deviations do not affect the scientific soundness or acceptability of the study.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided. This study was conducted in accordance with the GLP as published in 40 CFR Part 160 with the following exceptions: the stability, homogeneity, verification of the test substance concentration in the dosing solutions were not determined, and periodic analyses of feed and water for potential contaminants were not conducted in accordance with GLP, but were performed using a certified laboratory and standard U.S. EPA analytical methods.

A. MATERIALS:

1. Test Material DPX-MAT28 Technical (aminocyclopyrachlor)

Description: Solid

Lot No./Batch No.: Not reported

Purity: 92.2%

Stability of compound under test conditions: Stability experiments were not conducted.

Storage conditions of test chemicals: Ambient conditions

Physicochemical properties of Aminocyclopyrachlor.

Parameter	Values	Comments
Water solubility at 20°C	Not reported	
Vapor pressure	Not reported	
UV absorption	Not reported	
pKa	Not reported	
Kow	Not reported	

(OECD recommends water solubility, stability in water and light, pKa, Pow, and vapor pressure of test compound)

2. Test Organism:

Species (common and scientific names): Northern bobwhite quail (*Colinus virginianus*)

Age at study initiation: Young adult, *ca.* 20 weeks old

Weight at study initiation (mean and range): males – 179 to 221 g; females – 168 to 219 g

Source: Buckeye Gamebirds, Defiance, OH

(EPA recommends using either bobwhite quail or mallard duck. Birds should be at least 16 weeks old at test initiation and should be uniform in size and weight as well as phenotypically indistinguishable from wild birds).

B. STUDY DESIGN:

1. Experimental Conditions

a. Range-finding study: None reported. Test dosages were established based upon available toxicity information provided by the Sponsor.

b. Definitive study

Table 1: Experimental Parameters

Parameter	Details	Remarks *Criteria*
Acclimation Period:	*Ca.* 8 weeks	One day following arrival, test birds were given water-soluble antibiotics in their drinking water for 2 consecutive days. The use of medicated water was suspended for 5 days due to avoidance, then resumed for a 6-day period. During acclimation, all birds were observed at least daily, and any birds exhibiting abnormal behavior or physical injury were not used for testing. A detailed description of the diet was provided; the bird diet contained a minimum of 27% protein and 2.5% crude fat, and a maximum of 3.8% crude fiber. *The recommended acclimation period is a minimum of 15 days. OECD recommends a minimum of 7 days.*
Conditions: (same as test or not)	Same as test	
Feeding:	Game bird ration formulated to Wildlife International Ltd.'s specifications (by Cargill Animal Nutrition, Shippensburg, PA) and water from the town of Easton public water supply were offered *ad libitum*	
Health: (any mortality observed)	Not reported.	

Parameter	Details	Remarks *Criteria*
Pen size and construction materials	78 x 51 x 20/25 cm (sloping floors) pens were constructed of wire mesh (external walls, ceilings, and floors) and galvanized sheeting (side walls).	There was approximately 796 cm^2 floor space per bird. *Pen size and construction should conform to good husbandry practices and should not create crowding stress.* *OECD recommends that pens be suitable for the captive rearing of that species.*
Test duration	14 days	*Recommended test duration is one day for dosing and at least 14 days observation.*
Dose preparation [Indicate method of confirmation of dose]	The test substance was ground with a mortar and pestle, then mechanically dispersed in 1% aqueous carboxymethyl cellulose (CMC) solution.	
Mode of dose administration	Gavage	*Gavage or gelatin capsule is recommended*
Dose levels nominal: measured:	0 (vehicle control), 269, 448, 747, 1245, and 2075 mg ai/kg bw Not verified	The dosages were adjusted for the purity of the test substance. *Dose levels should be a minimum of 5 treatment levels unless LD_{50} is demonstrated to be greater than 2000 mg ai/kg*
Solvent/vehicle, if used type: amount/bw:	1% aqueous CMC solution 4 mL/kg bw	*The test material should be administered without a vehicle if possible. Maximum vehicle should not exceed 0.1 to 1.0% of body weight.*
Number of birds per groups/treatment for negative control: for solvent/vehicle control: for treated:	N/A 10 (5 per sex) 10 (5 per sex)	*Recommended number of birds in a treatment group is 10 and 10 birds for each control and vehicle group.*

Parameter	Details	Remarks *Criteria*
No. of feed withholding days before dosing	*Ca.* 17 hours	*Food should be withheld for at least 15 hours prior to dosing.*
Test conditions Temperature: Relative humidity: Photoperiod:	 23.7 ± 0.3°C 34 ± 11% 8 hours light/16 hours dark	The birds were exposed to an average of approximately 196 lux of illumination. *The recommended photoperiod is 8 hours of light and 16 hours of dark.*
Reference chemical, if used name: concentrations tested:	None tested	

2. Observations:

Table 2: Observations

Criteria	Details	Remarks *Criteria*
Parameters measured (mortality/individual body weight at test initiation and termination/ mean feed consumption/ others)	- Mortality - Clinical signs of toxicity - Food consumption - Body weight	*Body weight should be measured at test initiation, on day 14 and at the end of the test if the test is extended beyond 14 days. Mortality should not be more than 10% in controls.* *Feed consumption should be measured as average daily food consumption.*
Indicate if the test material was regurgitated	None indicated	*Regurgitation is an indication that the dose was rejected. If this problem persists, the test should be repeated.*
Groups on which necropsies were performed	None	*Gross necropsies should be performed with inspections of the GI tract, liver, kidneys, heart, and spleen.*

Criteria	Details	Remarks *Criteria*
Observation intervals	Mortality and signs of toxicity were observed multiple times following dosing and at least twice daily thereafter. Body weights were measured individually on Days 0, 3, 7, and 14. Average food consumption was estimated for Days 0 to 3, 4 to 7, and 8 to 14.	
Were raw data included?	Yes.	

II. RESULTS AND DISCUSSION:

A. MORTALITY:

No mortalities were observed during the 14-day observation period. The 14-day LD_{50} was >2075 mg ai/kg bw, and the NOAEL for mortality was 2075 mg ai/kg bw.

Table 3: Effect of DPX-MAT28 Technical (Aminocyclopyrachlor) on Mortality of Northern Bobwhite Quail.

Treatment (mg ai/kg bw)		No. of Birds	Cumulative Mortality				
			day 3	day 5	day 7	day 10	day 14
Vehicle control		10	0	0	0	0	0
269		10	0	0	0	0	0
448		10	0	0	0	0	0
747		10	0	0	0	0	0
1245		10	0	0	0	0	0
2075		10	0	0	0	0	0
NOAEL		2075 mg ai/kg bw					
LD_{50} (95% C.I.)		>2075 mg ai/kg bw					
Reference chemical	mortality	N/A					
	LD_{50}	N/A					
	NOAEL	N/A					

B. SUBLETHAL TOXICITY ENDPOINTS:

No overt signs of toxicity were observed at any treatment level. Incidental injuries were noted for four birds during the study: three males in the 269 mg ai/kg bw level and one male in the 448 mg ai/kg bw level were noted with foot lesions during the final 2 days of the study. Aside from the incidental injuries, all birds were normal in appearance and behavior during the 14-day observation period. The NOAEL for clinical signs of toxicity was 2075 mg ai/kg bw.

Based upon visual interpretation of the data, there were no apparent treatment-related effects at any level for body weight or feed consumption in either sex. The NOAEL for body weight and food consumption endpoints were 2075 mg ai/kg bw.

Table 4: Sublethal Effect of DPX-MAT28 Technical (Aminocyclopyrachlor) on Northern Bobwhite Quail.

Mean Body Weight Change, g								
Treatment, (mg ai/kg bw)	**Males**				**Females**			
	Days 0-3	**Days 3-7**	**Days 7-14**	**Days 0-14**	**Days 0-3**	**Days 3-7**	**Days 7-14**	**Days 0-14**
Vehicle control	2	-3	7	6	0	1	5	6
269	2	-2	-3	-3	2	0	5	8
448	0	0	3	3	3	-1	5	7
747	2	-2	5	5	2	0	5	7
1245	3	0	5	8	1	1	7	9
2075	2	2	6	10	2	-2	6	7
NOAEL	2075 mg ai/kg bw							
EC_{50}	>2075 mg ai/kg bw							

Mean Feed Consumption, g/bird/day						
Treatment, (mg ai/kg bw)	**Males**			**Females**		
	Days 0-3	**Days 4-7**	**Days 8-14**	**Days 0-3**	**Days 4-7**	**Days 8-14**
Vehicle control	28	27	22	15	16	16
269	24	24	21	22	22	20
448	16	17	16	20	19	19
747	17	17	17	25	25	23
1245	20	19	19	22	23	23
2075	15	16	16	15	15	15
NOAEL	2075 mg ai/kg bw					
EC_{50}	>2075 mg ai/kg bw					

C. REPORTED STATISTICS:

The 14-day LD_{50} value was determined to be greater than the highest dosage tested. No statistical analyses were applied to separate mean responses among treatment groups for body weight or food consumption.

D. VERIFICATION OF STATISTICAL RESULTS:

Statistical Method: Statistical analyses were not required to verify the results of this study. There was no mortality and body weight and food consumption were clearly not affected by treatment in any dose-dependent manner.

LD_{50}: >2075 mg ai/kg bw 95% C.I.: N/A
Probit slope: N/A 95% C.I.: N/A
NOAEL: 2075 mg ai/kg bw
Endpoint(s) Affected: none

E. STUDY DEFICIENCIES:

There were no significant deviations from U.S. EPA OPPTS Guideline No. 850.2100 affecting the scientific soundness or acceptability of this study.

F. REVIEWER'S COMMENTS:

The reviewer's conclusions agreed with the study authors.

Experiment study dates were March 23 to April 6, 2007.

G. CONCLUSIONS:

This study is scientifically sound and is classified as acceptable. No treatment-related mortality, clinical signs of toxicity, or effects on body weight or food consumption were indicated following a single oral dose of DPX-MAT28 Technical (aminocyclopyrachlor) to Northern bobwhite quail at levels up to and including the limit dose. The 14-day LD_{50} was >2075 mg ai/kg bw, and the NOAEL was 2075 mg ai/kg bw.

LD_{50}: >2075 mg ai/kg bw 95% C.I.: N/A
Probit slope: N/A 95% C.I.: N/A
NOAEL: 2075 mg ai/kg bw
Endpoint(s) Affected: none

III. REFERENCES:

U.S. Environmental Protection Agency. 1982. *Avian Single-Dose oral LD50 Test,* Pesticide Assessment Guidelines, FIFRA Subdivision E, Hazard Evaluation: Wildlife and Aquatic Organisms, Subsection 71-1. Environmental Protection Agency, Office of Pesticide Programs, Washington, D.C.

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